## REMARKS

Claims 18-21, 30, 32, 40-41, 52, 56-58 and 80-82 are pending.

## Information Disclosure Statement

Applicant filed an Information Disclosure Statement on April 30, 2008. The Examiner sent the Applicant a Non-Final Office Action on July 7, 2008 enclosing copies of Information Disclosure Statements initialed by the Examiner as being acknowledged. However, under Non Patent Literature Documents, the Examiner did not initial the citation for the European Search Report, European Application No. 03 78 6836, dated 3/19/08. Applicants again request that the Examiner return a copy of the initialed Information Disclosure Statement to confirm that this document has been considered.

## Rejections under 35 U.S.C. §102

The Examiner rejected claims 18-21, 30, 32, 40-41, 56-58, 80 and 82 under 35 U.S.C. §102(a) as being anticipated by Sirhan et al. (WO 2002/056790).

Independent claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is released upon degradation of the first polymer. Claims 18-21, 30, 32, 40-41, 56-58 and 82 depend directly or indirectly from claim 80.

35 U.S.C. §102(a) provides that an invention is not novel if "the invention was . . . described in a printed publication . . . before the invention thereof by the applicant." In order to demonstrate anticipation, one must show "that the four corners of a single, prior art document describe every element of the claimed invention." *Net Moneyin, Inc. v. Verisign*, 545 F.3d 1359, 1369, 88 USPQ2d 1751 (Fed. Cir. 2008) (citing *Xerox Corp. v. 3Com Corp.*, 458 F.3d 1310, 1322, quoting *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000)). The court in *Verisign* went on to state that "because the hallmark of anticipation is prior invention, the prior art reference – in order to anticipate under 35 U.S.C. §102 – must not only

disclose all elements of the claim within the four corners of the document, but must also disclose those elements 'arranged as in the claim.'" *Verisign* at 1370. The court explained

> The meaning of the expression "arranged as in the claim" is readily understood in relation to claims drawn to things such as ingredients mixed in some claimed order. In such instances, a reference that discloses all of the claimed ingredients, but not in the order claimed, would not anticipate, because the reference would be missing any disclosure of the limitations of the claimed invention "arranged as in the claim." But the "arranged as in the claim" requirement is not limited to such a narrow set of "order of limitations" claims. Rather, our precedent informs that the "arranged as in the claim" requirement applies to all claims and refers to the need for an anticipatory reference to show all of the limitations of the claims arranged or combined in the same way as recited in the claims, not merely in a particular order. The test is thus more accurately understood to mean "arranged or combined in the same way as in the claim."

Therefore, the reference must "clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures...." *In re Arkley,* 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (CCPA 1972). In *Arkley*, a prior art reference generically disclosed a class of compounds, which encompassed the claimed compound and a very large number of other compounds. While it was argued the prior art also disclosed two precursors of the claimed compound in the examples, the court found no anticipation under § 102. Specifically, the court found that the prior art examples disclosed the precursors only to the extent that one skilled in the art would have selected a specific acid to react with a particular tertiary amine. In its holding, the court stated there was nothing in the reference that "'clearly and unequivocally' directs those skilled in the art to make this selection...." *In re Arkley,* 455 F.2d 586, 587, 172 U.S.P.Q. 524, 526 (CCPA 1972).

Similar to *Arkley*, Applicant respectfully asserts that the pending claims are not anticipated because Sirhan et al. does not "clearly and unequivocally" direct one skilled in the art to select and combine the elements of the claimed invention. Sirhan et al. discusses luminal prostheses that allow for controlled release of at least one therapeutic capable agent. Sirhan et al., Abstract. Sirhan et al. suggest that the source of the therapeutic capable agent could be a polymeric material including therapeutic capable agent moieties as a structural subunit of the polymer. Sirhan et al. at page 8, paragraph [30] and page 29, paragraph [113]. Sirhan et al. incorporates by reference WO 99/12990 (Uhrich), which discloses the use of salicylic acid in a

polymer backbone, with salicylic acid being released upon degradation via hydrolysis of the polymer backbone. WO 99/12990 at page 18, Example VIII. However, Sirhan et al. do not clearly and unequivocally direct this selection—Sirhan et al. provide numerous methods to achieve controlled release of at least one therapeutic agent, as exemplified by the Examples. In Examples 1, 2, 3, and 8 of Sirhan et al. a drug was loaded onto a stent by spraying or dipping, and then a copolymer or barrier was deposited over the drug. In Example 4, a matrix solution including a matrix polymer and a therapeutic capable agent was coated onto a stent, and the stent was then coated or sprayed with a top coat of a rate-controlling barrier. In Example 7, a matrix solution including a matrix polymer (CAB) and a therapeutic capable agent (mycophenolic acid) were coated onto a stent, and the stent was then coated or sprayed with a top coat of a rate-controlling barrier (parylene). It should be noted that Sirhan et al. did not actually prepare any devices comprising a polymer with an active agent incorporated into the polymer backbone.

Sirhan et al. also discloses "another therapeutic capable agent" may be used, possibly acting in synergy with the first therapeutic agent. Sirhan et al. at page 11, paragraphs [40] and [41]. This secondary agent may be administered by a wide variety of methods. The second compound "may be administered prior to, concurrent with, or subsequent to the implanting of the device (e.g., prosthesis) of the present invention" Sirhan et al. at page 16, paragraph [62]. For example, the second agent "may be associated with expandable structure in the same or different manner as the first therapeutic capable agent." Sirhan et al. at page 11, paragraph [40]. Alternatively, the second compound may be in the form of a tablet to be taken orally, a transdermal patch to be placed on the patient's skin, subcutaneously, systemically by direct introduction to the blood stream, by way of inhalation, or through any other pathways and bodily orifices, or may be made available to the intracorporeal body by a catheter. Sirhan et al. at page 16, paragraph [63]; pages 40-41, paragraph [159]. Furthermore, Sirhan et al. discusses a wide array of compounds that could be used as the second therapeutic agent. Specifically, in paragraph 42, Sirhan et al. enumerates a combination of over 25 broad classes of drugs and specific compounds that could generally be used as the second therapeutic agent. Additionally, when discussing individual or daily doses to achieve a bollus level of the agent, Sirhan et al. states the second compound could be mycophenolic acid or rapamycin. Paragraph 65 at page 17. Therefore, Sirhan et al. do not clearly and unequivocally direct rapamycin be dispersed in a polymer matrix, wherein salicylic acid is incorporated into the backbone of the polymer.

Applicant submits that Sirhan et al. does not clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without any need for picking, choosing and combining various disclosures. Sirhan et al. discuss the coating of a therapeutic capable agent onto a stent along with the possibility of administering a second therapeutic agent. While Sirhan et al. disclose numerous drugs that could be used as the secondary agent, specifically using rapamycin as a second compound is only mentioned in a discussion of achieving a bullous level. Sirhan et al. do not "clearly and unequivocally" or "without any need for picking, choosing and combining various disclosures not directly related to each other" teach that rapamycin could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer.

Thus, Applicant respectfully asserts that the pending claims are not anticipated by Sirhan et al., and request the withdrawal of the rejection of claims 18-21, 30, 32, 40-41, 56-58, 80 and 82.

Additionally, it is noted that claim 52 is not included at page 2 of the Office Action in the list of claims that are rejected under 35 U.S.C. §102(a) as being anticipated by Sirhan et al. However, claim 52 is referenced by the Examiner at page 4, line 1 of the Office Action. If the rejection under 35 U.S.C. §102(a) over Sirhan et al. is maintained, Applicant requests that the Examiner clarify whether claim 52 is included in the rejection.

**Rejections under 35 U.S.C. §103(a)**

The Examiner rejected claims 18-21, 30, 32, 40-41, 52, 56-58 and 80-82 under 35 U.S.C. §103(a) as being unpatentable over Sirhan et al. (WO 2002/056790) in view of Ragheb et al. (US 6,730,064).

As discussed above, claim 80 recites a medical device having at least one surface, comprising: 1) a first polymer comprising salicylic acid incorporated into the polymer backbone on all or a portion of the surface, wherein the salicylic acid is disassociated from the polymer upon hydrolysis; and 2) a second active agent selected from paclitaxel and rapamycin that is dispersed within the polymer matrix of the first polymer such that the second active agent is

released upon degradation of the first polymer. Claims 18-21, 30, 32, 40-41, 56-58 and 81-82 depend directly or indirectly from claim 80.

An obviousness determination turns on underlying factual inquires involving: (1) the scope and content of prior art, (2) differences between claims and prior art, (3) the level of ordinary skill in pertinent art, and (4) secondary consideration s such as commercial success and satisfaction of a long-felt need. *Graham v. John Deere Co.,* 383 U.S. 1, 17 (1966). The Supreme Court has explained that the Federal Circuit's "teaching, suggestion or motivation" test provides helpful insight into the obviousness question as long as it is not applied rigidly. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 127, S. Ct. 1727, 1741 (2007). Accordingly, under *KSR*, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chem. Indus., Ltd., v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007).

The MPEP at §2142 states the following regarding determining obviousness under 35 U.S.C. §103:

> [t]he examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of an Applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences," conduct the search, and evaluate the "subject matter as a whole" of the invention. The tendency to resort to "hindsight" based upon an Applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

As discussed above, Sirhan et al. do not teach all of the elements of the present invention. Sirhan et al. do not "clearly and unequivocally" or "without any need for picking, choosing and combining various disclosures not directly related to each other" teach that rapamycin could be dispersed within the polymer matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, such that polymer comprising salicylic acid incorporated into the polymer backbone is released upon degradation of the salicylic acid polymer, as recited by claims 18-21,

30, 32, 40-41, 52, 56-58, 80 and 82. Furthermore, Sirhan et al. provide no motivation to select and combine the elements of the claimed invention, and given the disclosure, one skilled in the art would have no reasonable expectation of success with this endeavor. As stated above, Sirhan et al. discuss numerous methods for achieving the controlled release of at least one therapeutic agent and enumerate broad classes of compounds that could be employed as the primary or secondary agent. Sirhan et al. provide no motivation to select salicylic acid as a primary therapeutic agent, to incorporate the salicylic acid into the backbone of a polymer, to select rapamycin as a second therapeutic agent and to disperse the rapamycin throughout the polymer matrix. It would only be through impermissible hindsight that the claimed invention would have been obvious to one skilled in the art looking to Sirhan et al.

Ragheb et al. do not remedy the deficiencies of Sirhan et al. Ragheb et al. teach a vascular stent or other implantable medical device that provides a controlled release of a bioactive material into the vascular or other system, or other location in the body, in which a stent or other device is positioned. Ragheb et al. at col. 3, lines 8-13. Ragheb et al. teach positing a coating layer on one surface of the device, positing the bioactive material over the coating layer so that the coating layer provides for a controlled release of the bioactive material, and then positing a porous layer over the bioactive material, where the porous layer also provides for a controlled release of the bioactive material through the porous layer. Ragheb et al. at col. 3, lines 16-24. Ragheb et al. state that "a vast range of drugs, medicaments and materials may be employed as the bioactive material in the layer" (Ragheb et al. at col. 8, lines 7-10), and indicate that paclitaxel could be coated onto stents (Ragheb et al. at col. 14, lines 36-37).

The Examiner attempts to argue that it would have been obvious to use paclitaxel, as disclosed by Ragheb et al., as the secondary therapeutic agent of Sirhan et al. As stated above, Ragheb et al. disclose a vast range of drugs and one skilled in the art would have no motivation to select paclitaxel. Even if paclitaxel were selected, there is no motivation or teaching in either Sirhan et al. or Ragheb et al. to select every element of the claimed invention and combine the elements in the recited fashion. Only through hindsight would it have been obvious to disperse paclitaxel into the matrix of a polymer comprising salicylic acid incorporated into the polymer backbone, as recited by claim 81.

Singly or combined, Sirhan et al. and Ragheb et al. do not teach or suggest that paclitaxel or rapamycin be incorporated into the matrix of a polymer comprising salicylic acid incorporated

into the polymer backbone, as recited by the instant claims. Applicant respectfully asserts that claims 18-21, 30, 32, 40-41, 52, 56-58 and 80-82 are not obvious over Sirhan et al. in view of Ragheb et al., and respectfully requests that this rejection be withdrawn.

## CONCLUSION

The Examiner is invited to contact Applicant's Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby.

**If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.**

Respectfully submitted,

Date: 13 July 2010

By: _____

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